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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/332,803	06/14/1999	RONALD VOGELS	4075US	3357

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EXAMINER	
GUZO, DAVID	
ART UNIT	**PAPER NUMBER**
1636	23

DATE MAILED: 11/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/332,803	VOGELS, RONALD	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/10/01, 2/7/02, 3/18/02 and 3/21/03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3, 6, 8, 10, 13, 14, 16, 17, 60, 62, 66, 69, 70, 72 and 73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *16,17,72 and 73* is/are allowed.

6)☒ Claim(s) *3,6,8,10,13,14,60,62,66,69 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6, 8, 14, 60, 62 and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by Berkner or Stratford-Perricaudet et al.

Both applicants and Berkner (Curr. Top. Micro. Immuno., 1992, Vol. 158, see whole article, particularly pp. 47-50) as well as Stratford-Perricaudet et al. (Human gene Transfer, 1991, Vol. 219, pp. 51-61, see whole article, particularly pp. 52 and 55) recite a method for generating adenoviral vectors comprising the same method steps, i.e. welding together two nucleic acid molecules (by a single homologous recombination event), wherein said nucleic acid molecules comprise partially overlapping sequences, wherein each nucleic acid is incapable of replicating in mammalian cells, each can comprise an ITR, overlapping sequences, etc. and wherein the resultant vector produced as a result of the welding together comprises two ITRs, an encapsidation sequence, a gene of interest, optionally the E2 and/or E4 regions, wherein one of the adenovirus ITRs is essentially free of other nucleic acid, etc. It is noted that the two nucleic acids cannot form replication competent adenoviruses as adenoviral sequence essential for generation of replication competent adenoviruses (i.e. E1 sequences) are not present in either nucleic acid molecule. Therefore, Berkner and Stratford-Perricaudet et al. both teach the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 6, 8, 13, 14, 60, 62, 69 and 70 are rejected under 35 U.S.C. 102(e) as being anticipated by Fallaux et al. (U.S. Patent 5,994,128).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Applicants' invention is as described in the above 35 USC 102(b) rejection. In addition, claims 13 and 69 recite a method of generating an adenoviral vector comprising homologous recombination between two different adenovirus nucleic acid molecules in PER.C6 cells.

Fallaux et al. (previously cited, see whole document, particularly Figs. 11-12, columns 6, 17-18 and Table II) recites the same methods for generating recombinant adenoviral vectors that are claimed by applicants and teaches that PER.C6 cells can be used to generate recombinant adenoviral vectors whereby the PER.C6 cells are

transfected with adenoviral vectors comprising overlapping sequences and wherein homologous recombination is used to generate the adenoviral vector in the absence of replication competent adenoviruses. Fallaux et al. therefore teaches the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10 and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berkner.

Applicants claim a method for generating recombinant adenovirus vectors comprising welding together two nucleic acid molecules by homologous recombination

wherein at least one of the nucleic acid molecules comprises an ITR made essentially free of other nucleic acid on one side using a restriction endonuclease.

Berkner (previously cited by the examiner, see whole article, particularly pp. 47-51) teaches the same homologous recombination methodologies to generate recombinant adenoviral vectors. Berkner also teaches that adenoviral genomic or subgenomic sequences are often cloned using plasmid vectors such as pBR322 and that cleavage between the bacterial vector plasmid and the left or right adenoviral ITR (e.g. at linker sequences attached to the adenoviral ITRs) is necessary for infectivity. The ordinary skilled artisan, seeking to generate adenoviral vector sequences suitable for transfection into cells so as to generate infectious adenoviral vectors would have been motivated to cleave with restriction endonucleases the adenoviral sequences from any cloning plasmid that may have been used to clone and manipulate said adenoviral sequences so that the adenoviral vectors so generated would be infectious. It would have been obvious for the ordinary skilled artisan to do this because the adenoviral vector sequences need to cleaved from the cloning plasmid sequences in order to be infectious. Given the teachings of the cited prior art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

> art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13 and 69 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants have responded (on 2/7/02) to this rejection by submitting a Deposit Declaration. However, the Declaration is deficient because the deposit was made after the effective filing date of the application but the Declaration does not comply with 37 CFR 1.804(b). Specifically, the Declaration did not include a statement that the biological material which is deposited is the biological material specifically identified in the application as filed. It is noted that the instant Declaration appears to be a duplicate of the Declaration previously submitted (on 7/2/01). The rejection will be maintained until a suitable Deposit Declaration is received.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 6, 13, 14, 62, 69 and 70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 6, 13, 14, 62, 69 and 70 are vague in that applicants recite two nucleic acid sequences which have overlapping homologous sequences which recombine in a cell to form a single physically linked adenoviral vector molecule but do not include

sequence overlap leading to formation of replication competent adenovirus. The configuration of the overlapping sequences is indefinite in that it is unclear how overlapping sequences on the two molecules can, on the one hand, lead to homologous recombination in order to generate a recombinant adenovirus vector but not generate a replication competent adenoviral vector, i.e. are sequences essential for generating replication competent virus absent from the two molecules?

Claim 3 is vague in the recitation of the phrase "...both nucleic acid molecule...". The word "molecule" should be plural. Claim 3 is also vague in that applicants recite a method for generating an adenoviral vector comprising at least two ITRs but the method steps only involve welding together two nucleic acid molecules which possess only one ITR. It is unclear where the second ITR in the adenoviral vector came from.

Applicants submitted (on 2/7/02) a certified copy of patent application No. 95201728.3, filed 06/26/1995, and applicants indicate that this is a priority for the instant application. However, applicants do not claim benefit for this document anywhere in the instant application. Applicants only claim benefit for the parent application 09/065,752, filed 04/24/98. Applicants are therefore not granted benefit for the 95201728.3 application which was filed more than one year prior to the filing date of the 09/065,752 application.

Any rejections not repeated in this Office Action are withdrawn.

Claims 16-17 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (703) 308-7307. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

David Guzo
November 19, 2003